

Original citation:

Tselepy, Ashton, Schiller, Tara L., Harrisson, Simon, Guerrero-Sanchez, Carlos, Moad, Graeme and Keddie, Daniel J. (2018) Effect of scandium triflate on the RAFT copolymerization of methyl acrylate and vinyl acetate controlled by an acid/base “switchable” chain transfer agent. *Macromolecules*, 51 (2). pp. 410-418.

Permanent WRAP URL:

<http://wrap.warwick.ac.uk/100887>

Copyright and reuse:

The Warwick Research Archive Portal (WRAP) makes this work by researchers of the University of Warwick available open access under the following conditions. Copyright © and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable the material made available in WRAP has been checked for eligibility before being made available.

Copies of full items can be used for personal research or study, educational, or not-for profit purposes without prior permission or charge. Provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

Publisher's statement:

This document is the Accepted Manuscript version of a Published Work that appeared in final form in *Macromolecules*, copyright © American Chemical Society after peer review and technical editing by the publisher.

To access the final edited and published work see

<http://dx.doi.org/10.1021/acs.macromol.7b02104>

A note on versions:

The version presented here may differ from the published version or, version of record, if you wish to cite this item you are advised to consult the publisher's version. Please see the 'permanent WRAP url' above for details on accessing the published version and note that access may require a subscription.

For more information, please contact the WRAP Team at: wrap@warwick.ac.uk

The Effect of Scandium Triflate on the RAFT Copolymerization of Methyl Acrylate and Vinyl Acetate Controlled by an Acid/Base “Switchable” Chain Transfer Agent.

*Ashton Tselepy,^a Tara L. Schiller,^b Simon Harrison,^c Carlos Guerrero-Sanchez,^{d,e} Graeme Moad,^d Daniel J. Keddie^{*a,d,f}*

^aChemistry, School of Science and Technology, University of New England, Armidale, NSW, 2351, Australia.

^bInternational Institute of Nanocomposites Manufacturing, WMG, University of Warwick, CV4 7AL, United Kingdom.

^cIMRCP, UMR CNRS 5623, Université de Toulouse, 118 route de Narbonne, 31062 Toulouse Cedex 9, France

^dCSIRO Manufacturing Flagship, Bag 10, Clayton South, VIC 3169, Australia.

^eLaboratory of Organic and Macromolecular Chemistry (IOMC) & Jena Center for Soft Matter (JCSM), Friedrich Schiller University Jena and Polymer Libraries GmbH, Philosophenweg 7, 07743 Jena, Germany

^fSchool of Sciences, Faculty of Science & Engineering, University of Wolverhampton, Wulfruna Street, Wolverhampton, WV1 1LY, United Kingdom

ABSTRACT: Modulation of the activity of an acid/base switchable dithiocarbamate RAFT agent, cyanomethyl (4-fluorophenyl)(pyridin-4-yl)carbamodithioate, with the Lewis acid scandium triflate (Sc(OTf)₃) was investigated to examine the ability to deliver improved control over RAFT copolymerizations involving both more-activated and less-activated monomers – specifically the copolymerization of methyl acrylate (MA) and vinyl acetate (VAc). The introduction of either 0.5 or 1

molar equivalents of $\text{Sc}(\text{OTf})_3$, with respect to RAFT agent, into a RAFT copolymerization of MA and VAc provides substantially improved control resulting in significantly reduced molar mass dispersities (\bar{D}) (~ 1.1 - 1.3) than achieved in its absence (ca. $\bar{D} \sim 1.3$ - 1.4). Furthermore, similar introduction of $\text{Sc}(\text{OTf})_3$ into MA homopolymerization mediated by the same RAFT agent also delivered polymers of very low \bar{D} (~ 1.15). $\text{Sc}(\text{OTf})_3$ was also found to lower the rate of polymerization, and alter the copolymerization reactivity ratios for MA and VAc. Increasing the Lewis acid concentration provides enhanced incorporation of the less active monomer, VAc, into the copolymers ($[\text{Sc}(\text{OTf})_3]/[\text{RAFT}] = 0$, $r_{\text{MA}} = 4.04$, $r_{\text{VAc}} = 0.032$; $[\text{Sc}(\text{OTf})_3]/[\text{RAFT}] = 0.5$, $r_{\text{MA}} = 3.08$, $r_{\text{VAc}} = 0.17$; $[\text{Sc}(\text{OTf})_3]/[\text{RAFT}] = 1$, $r_{\text{MA}} = 2.68$, $r_{\text{VAc}} = 0.62$). Carbon nuclear magnetic resonance (^{13}C NMR) and differential scanning calorimetry (DSC) analysis of preparative samples confirm the enhanced VAc incorporation with increased levels of $\text{Sc}(\text{OTf})_3$. Importantly the inclusion of $\text{Sc}(\text{OTf})_3$ does not deleteriously affect the thiocarbonylthio end-groups of the RAFT polymers, with high end-group fidelity being observed in all copolymerizations.

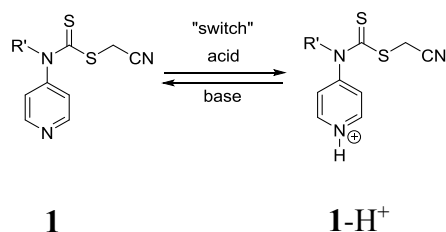
INTRODUCTION

In circumstances where a conventional radical copolymerization normally results in a blend of compositionally distinct polymers due to compositional drift in the monomer feed,¹ copolymerization by reversible deactivation radical polymerization (RDRP) provides a homogeneous gradient copolymer.¹⁻⁷ In a standard batch process, the relative steepness of the gradient along each polymer chain is determined by the relative reactivity of each of the monomers during polymerization (i.e. the copolymerization reactivity ratios, r_1 and r_2); in general a greater difference between r_1 and r_2 leads to a steeper gradient.

For preparation of well-defined polymers that incorporate both “more activated monomers” (MAMs, i.e. (meth)acrylates, (meth)acrylamides, styrenes) and “less activated monomers” (LAMs, i.e. vinyl esters, vinylamides), which have vastly different reactivities in radical polymerization, RAFT is the most appealing of the RDRP techniques. Due to its degenerative transfer mechanism RAFT can deliver well defined polymers of either MAMs or LAMs by tailoring of the structure of the thiocarbonylthio RAFT agent ($\text{ZC}(=\text{S})\text{SR}$).⁸ Indeed block copolymers of MAMs and LAMs with defined molar mass and low

dispersity (\bar{D}) have been synthesised using acid/base “switchable” *N*-4-pyridinyl dithiocarbamate RAFT agents (see Scheme 1).⁹⁻¹²

Scheme 1: Acid/Base “switchable” RAFT agents (where **1** controls the polymerization of LAMs; **1-H⁺** controls the polymerization of MAMs)



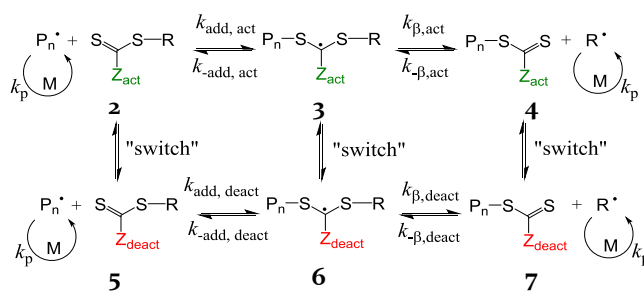
The case of statistical copolymerization of MAMs and LAMs is more complex. In the presence of a lower activity RAFT agent (low chain transfer coefficient (C_{tr})) such as an *O*-alkyl xanthate ($Z=OR'$), *N*-alkyl-*N*-aryldithiocarbamate ($Z=NR'Ar$) or *N*-alkyl-*N*-pyridinyldithiocarbamate ($Z=NR'-4-Py$) the rate of addition of the propagating MAM-derived radical to the thiocarbonyl is low. This results in many propagation events per active cycle and gives polymers of relatively high \bar{D} . Conversely, when attempting the polymerization of a LAM in the presence of a high activity RAFT agent such as a dithioester ($Z=R'$ or Ar) or trithiocarbonate ($Z=SR'$ or SAr) inhibition typically occurs due to the slow fragmentation of the highly reactive, less stabilised LAM-based propagating radicals. Even if one concedes the possibility of favourable rates of cross propagation of $PLAM^\bullet$ to MAM versus degenerative chain transfer, issues associated with non-ideal RAFT equilibria such as slow fragmentation will inevitably arise when using these active RAFT agents in a polymerization involving LAMs. Clearly, if one wishes to control the polymerization of both MAMs and LAMs concurrently during copolymerization some balance with respect to RAFT agent structure must be sought.

Although it has been shown that certain dithiocarbamates and xanthates with intermediate activity provide control over MAM/LAM copolymerization (e.g. *N,N*-dimethylacrylamide (DMAM)/vinyl acetate (VAc) with either 3,5-dimethyl-1*H*-pyrazolecarbodithioates¹³ or 4-chloro-3,5-dimethyl-1*H*-

pyrazolecarbodithioates,¹⁴ $D \sim 1.2$, *tert*-butyl acrylate (*t*BuA)/VAc with pentafluorophenyl xanthate, $D \sim 1.3$),¹⁵ the degree of control achieved was not ideal. No detailed analysis was reported in this instance. However we can surmise that the reactivity ratios ensure that the MAM is consumed relatively rapidly. Retardation was observed in the latter stages of copolymerization when the monomer feed comprises only the LAM.

The ideal approach to obtain control over a copolymerization of MAMs and LAMs would encompass modulation of the RAFT agent activity, through an activation/deactivation process, during the polymerization reaction (see Scheme 2). Indeed this would facilitate both efficient addition of MAM-derived propagating radicals to the thiocarbonyl of the activated (macro)-RAFT agent (**2** or **4**) and promote fragmentation of LAM-derived propagating radicals from the less stabilised, deactivated RAFT intermediate (**6**).

Scheme 2: Proposed equilibria of Reversible-Addition Fragmentation Chain Transfer (RAFT) Polymerization and RAFT agent activation/deactivation via Lewis acid interaction



Acid/base equilibria involving Lewis basic “switchable” dithiocarbamate RAFT agents can be exploited in this context. As the hydrolytic sensitivity of LAM derived end-groups precludes use of protic acids,^{10, 16} we instead propose the use of the hydrolytically stable Lewis acid¹⁷ scandium triflate ($\text{Sc}(\text{OTf})_3$) to preserve the RAFT end-group during the polymerization. Rare earth triflates, including $\text{Sc}(\text{OTf})_3$, $\text{Yb}(\text{OTf})_3$ and $\text{Y}(\text{OTf})_3$, have previously been exploited to achieve stereocontrol in conventional radical polymerization¹⁸⁻²³ and RDRP.²³⁻²⁹ Additionally, the compatibility of Lewis acid switching with RAFT polymerization has been illustrated previously with aluminium triflate ($\text{Al}(\text{OTf})_3$).^{9, 30}

Herein, we describe the effect the Lewis acid $\text{Sc}(\text{OTf})_3$ has on molar mass, \bar{D} and the relative monomer reactivity during the RAFT homo- and copolymerization of methyl acrylate (MA) and vinyl acetate (VAc) (exemplar MAMs and LAMs respectively). Through estimation of the copolymerization reactivity ratios and by analysis the resultant copolymers by nuclear magnetic resonance (NMR) and differential scanning calorimetry (DSC) additional information on the distribution of each type of monomer unit along the polymer backbone was obtained.

EXPERIMENTAL

Materials.

All solvents were of analytical reagent grade unless otherwise stated. $\text{Sc}(\text{OTf})_3$, methyl acrylate (MA), VAc were purchased from Sigma-Aldrich and used as received unless otherwise stated. 2,2'-Azobis[2-methyl propionitrile] (AIBN) was purchased from Acros and purified by recrystallization twice from methanol prior to use. MA and VAc were filtered through neutral alumina activity I (70-230 mesh) and fractionally distilled under reduced pressure immediately before use. All deuterated solvents were obtained from Cambridge Isotope Laboratories. Cyanomethyl (4-fluorophenyl)(pyridin-4-yl)carbamodithioate (**8**),³¹ cyanomethyl *O*-ethyl carbonodithioate (**9**)³² and cyanomethyl dodecylcarbonotrithioate (**10**)³³ were prepared by the reported literature procedures.

Characterization.

NMR spectra were obtained with a Bruker Avance 300 or 400 MHz spectrometer. ^1H and ^{13}C NMR spectra were internally referenced to residual solvent.³⁴

Size exclusion chromatography (SEC) of poly(methyl acrylate) (PMA) and poly(methyl acrylate-*co*-vinyl acetate) (PMA-*co*-PVAc) was performed on a Shimadzu system equipped with a CMB-20A controller system, a SIL-20A HT autosampler, a LC-20AT tandem pump system, a DGU-20A degasser unit, a CTO-20AC column oven, a RDI-10A refractive index detector, 4 \times Waters Styragel columns (HT2, HT3, HT4 and HT5, each 300 mm \times 7.8 mm providing an effective molar mass range of 100-600000) and *N,N*-dimethylacetamide (DMAc) (containing 2.1 g L⁻¹ lithium chloride (LiCl)) at 80 °C (flow rate: 1 mL min⁻¹.

Number (M_n) and weight-average (M_w) molar masses were evaluated using Shimadzu LC Solution software. The SEC columns were calibrated with low dispersity polystyrene (PSt) standards (Polymer Laboratories) ranging from 3100 to 650000 g mol⁻¹ and molar masses are reported as PSt equivalents. A 3rd order polynomial was used to fit the log M_p vs. time calibration curve, which was linear across the molar mass ranges.

DSC was performed on a Mettler Toledo DSC1 (model 700) equipped with FRS5 thermocouple sensor and robotic sample changer. The copolymer samples were subjected to a heat-cool-heat protocol similar to that previously reported,⁴ with all temperature increments at 5 °C min⁻¹. The samples were first heated to 200 °C to erase thermal history and dry the samples of adsorbed water. Samples were then quenched to -40 °C before being reheated to 200 °C. Glass transition temperature (T_g) measurements were obtained from the second heating scan.

High-throughput RAFT polymerization experiments for kinetic analysis.

RAFT polymerization experiments for kinetic analysis were performed using a Chemspeed Swing-SLT automated synthesizer following procedures similar to those described elsewhere.^{7, 10, 35-40} The synthesizer was equipped with a glass reactor block consisting of 16 reaction vessels (13 mL) with thermal jackets connected in series through the reaction block and connected to a heating/cooling system (Hübler, -90 °C to 140 °C). In addition, all reaction vessels were equipped with cold-finger reflux condensers (~7 °C). Mixing was achieved by vortex agitation (up to 1400 rpm). Liquid transfers were handled by a 4-needle head (4-NH) capable of four simultaneous sample transfers. The 4-NH was connected to a reservoir bottle (degassed acetonitrile (MeCN)) for needle rinsing after each liquid transfer step. This solvent reservoir was degassed by continuously sparging with nitrogen and was also utilized to prime the tubing lines of the 4-NH. When experiments were carried out, the synthesizer was maintained under an inert atmosphere by supplying a constant flow of nitrogen into the hood of the synthesizer. A nitrogen atmosphere was also applied to reactors and stock solutions at all times. Prior to the polymerizations, to ensure an inert environment, the reaction vessels were heated to 135 °C and subjected to 10 cycles of vacuum (2 min) and

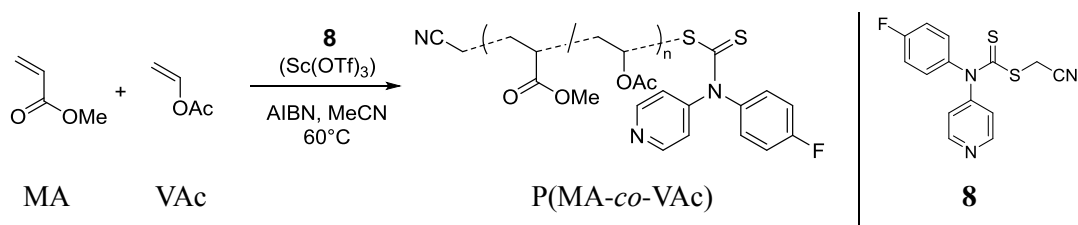
filling with nitrogen (2 min) to ensure the elimination of oxygen (see the supporting information (SI) for more details on the performed polymerization reactions).

RESULTS AND DISCUSSION

RAFT polymerization of methyl acrylate

Initially, to assess the ability of the Lewis acid, $\text{Sc}(\text{OTf})_3$, to activate the RAFT agent and facilitate enhanced control over the polymerization of the MAM MA, we employed **8**. We have previously shown this RAFT agent performs exceptionally in controlling the polymerization of both MA (when protonated) and VAc (when used neutral form).³¹

The polymerization of MA in the presence of **8**, without the addition of $\text{Sc}(\text{OTf})_3$, gave polymers of targeted molar mass with moderate \bar{D} , which is consistent with experiments previously reported³¹ (see Table 1, Entry 1 and Figure 1a). Upon addition of either 0.5 or 1 molar equivalent of $\text{Sc}(\text{OTf})_3$ with respect to RAFT agent concentration polymers of lowered \bar{D} were obtained, analogous to what is observed upon addition of protic acids³¹ (see Table 1, Entries 2, 3 and Figure 1a). In all cases the polymerization of MA in the presence of **8** showed a linear increase of molar mass with conversion, with molar masses above that calculated theoretically due to discrepancies introduced through the use of PSt SEC calibration standards. In the case of homopolymerization of MA there appears to be no significant difference between reactions performed with 0.5 or 1 molar equivalent of $\text{Sc}(\text{OTf})_3$ to RAFT agent **8**, suggesting that during polymerization the scandium centre may accommodate more than one RAFT-based pyridyl ligand.



Scheme 3: RAFT copolymerization of MA and VAc and the structure of RAFT agent **8**

Table 1: Synthesis of PMA, PVAc and P(MA-*co*-VAc) in acetonitrile (MeCN) at 60°C in the presence of **8** with varying amounts of Sc(OTf)₃^a

| Entry | f_{MA}^b | [Sc(OTf) ₃]/ [8] | Time (min) | MA conv. %. | VAc conv. %. | Total conv. %. | F_{MA}^c | F_{VAc}^c | M_n (calc.) ^d | M_n^e | \bar{D}^e |
|-------|-------------------|--|---------------|-------------------|--------------------|----------------------|-------------------|--------------------|-------------------------------|---------|-------------|
| 1 | 1 | 0 | 1440 | 99 | — | 99 | 1.0 | — | 17126 | 21100 | 1.3 |
| 2 | 1 | 0.5 | 1443 | 96 | — | 96 | 1.0 | — | 16569 | 26500 | 1.16 |
| 3 | 1 | 1 | 1445 | 95 | — | 95 | 1.0 | — | 16302 | 23500 | 1.15 |
| 4 | 0.75 | 0 | 1448 | 99 | 54 | 87 | 0.846 | 0.154 | 15053 | 19300 | 1.41 |
| 5 | 0.75 | 0.5 | 1450 | 91 | 45 | 79 | 0.858 | 0.142 | 13630 | 18400 | 1.29 |
| 6 | 0.75 | 1 | 1453 | 64 | 29 | 55 | 0.868 | 0.132 | 9535 | 13800 | 1.27 |
| 7 | 0.5 | 0 | 1455 | 100 | 53 | 77 | 0.653 | 0.347 | 13186 | 16400 | 1.38 |
| 8 | 0.5 | 0.5 | 1458 | 83 | 36 | 60 | 0.699 | 0.301 | 10259 | 12700 | 1.26 |
| 9 | 0.5 | 1 | 1460 | 72 | 54 | 63 | 0.574 | 0.426 | 10851 | 10000 | 1.21 |
| 10 | 0.25 | 0 | 1463 | 100 | 50 | 63 | 0.399 | 0.601 | 10772 | 12000 | 1.31 |
| 11 | 0.25 | 0.5 | 1465 | 77 | 27 | 40 | 0.482 | 0.518 | 6834 | 7570 | 1.13 |
| 12 | 0.25 | 1 | 1468 | 48 | 19 | 27 | 0.452 | 0.5 | 4595 | 5860 | 1.11 |
| 13 | 0 | 0 | 1470 | — | 28 | 28 | — | 1.0 | 4807 | 5670 | 1.12 |
| 14 | 0 | 0.5 | 1473 | — | 20 | 20 | — | 1.0 | 3515 | 1420 | 1.03 |
| 15 | 0 | 1 | 1475 | — | 0 | 0 | — | 1.0 | 0 | — | — |

^a[MA]+[VAc]:[**8**]:[AIBN] = 200:1.0:0.2, in MeCN, T = 60°C; ^b[MA]+[VAc] = 3.33 M; ^cCalculated from conversion data; ^d $M_n(\text{calc}) = ([\text{MA}]_0 + [\text{VAc}]_0)/[\text{RAFT}]_0 \times ((M_{r,\text{MA}} \times F_{\text{MA}}) + (M_{r,\text{VAc}} \times F_{\text{VAc}})) \times \text{total \% conv.} + M_{r,\text{RAFT}}$ (where F is the mole fraction of monomer in the polymer); ^eGPC DMF eluent, T = 80°C, LiCl = [50 mM]

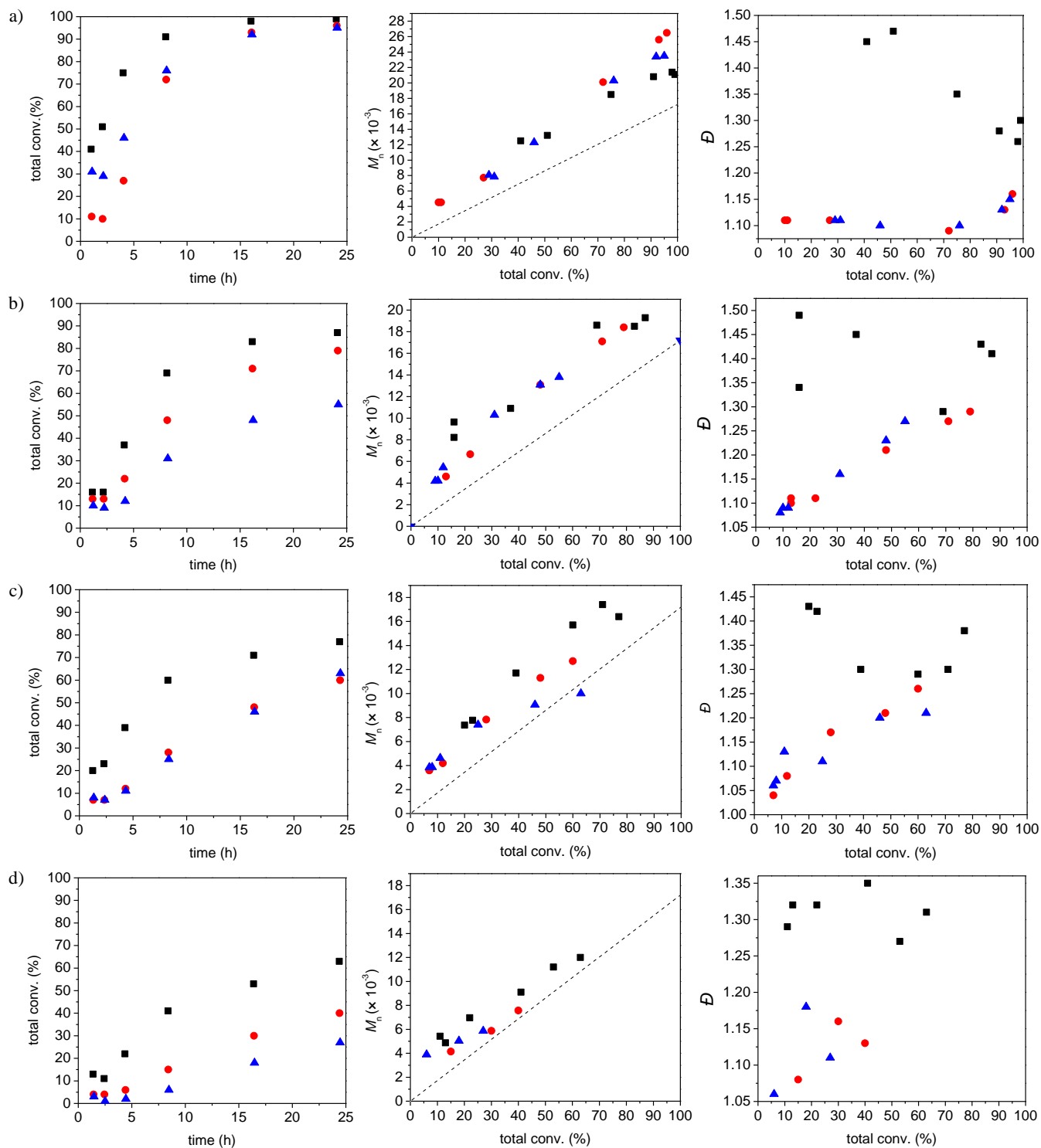


Figure 1: Total monomer conversion versus time plots (left), evolution of molar mass (M_n) with conversion (middle) and evolution of \bar{D} with total monomer conversion (right) for RAFT polymerizations in the presence of RAFT agent **8** for monomer feed ratios of (a) 100 % MA, (b) 75 % MA/25 % VAc, (c) 50 % MA/50 % VAc and (d) 25 % MA/75 % VAc with varying amounts of $\text{Sc}(\text{OTf})_3$, where $[\text{Sc}(\text{OTf})_3]/[\mathbf{8}]$: \blacksquare = 0; \bullet = 0.5; \blacktriangle = 1.0.

RAFT copolymerization of methyl acrylate and vinyl acetate

To investigate the effect of $\text{Sc}(\text{OTf})_3$ on the copolymerization of MAMs and LAMs in the presence of RAFT agent **8**, VAc (a model LAM) was introduced as comonomer alongside MA. Monomer feed ratios were varied between 75% MA/25% VAc, 50% MA/50% VAc and 25%MA/75% VAc whilst maintaining constant monomer, RAFT agent and initiator concentrations (see Table 1, Entries 4-12) allowing for calculation of monomer reactivity ratios (*vide infra*).

With 75% MA/25% VAc monomer feed the \bar{D} was observed to decrease with increasing $\text{Sc}(\text{OTf})_3$ concentration, coinciding with some rate retardation presumably caused by slower fragmentation of the PVAc propagating radicals from the coordinated RAFT intermediate (see Table 1, Entries 4-6, Figure 1b and Figure S1b). Additionally, a change in the relative rate of monomer incorporation was observed (see Table S1 for full details), suggesting an effect of $\text{Sc}(\text{OTf})_3$ on the monomer copolymerization reactivity ratios (*vide infra*). In the absence of $\text{Sc}(\text{OTf})_3$ \bar{D} decreased with monomer conversion (see Figure 1b, right). This is typical for acrylate polymerization in the presence of *N,N*-diaryldithiocarbamate RAFT agents^{31, 41} and is also consistent with that seen with 100% MA feed (see Figure 1a, right). In the presence of 0.5 or 1 molar equivalents of $\text{Sc}(\text{OTf})_3$ to RAFT agent **8** \bar{D} increases from low to moderate with conversion over the course of the reaction (see Figure 1b, right), due to the propensity for irreversible chain transfer and head-to-head addition in VAc polymerization.⁴² This is in contrast to the analogous experiments with 100% MA where \bar{D} was low throughout the polymerization (see Figure 1a, right). Instead these observations are akin to that typically observed for a well-controlled VAc polymerization using moderately active *N,N*-diaryldithiocarbamate^{41, 43-44} (and pyrazolecarbodithioate)¹³ RAFT agents.

The copolymerization reactions with 50% and 25% MA feeds (see Table 1, Entries 7-9 and 10-12 respectively) displayed similar trends with the polymerization rate retarded more with increased VAc

concentration (see Figure 1c and d). Inspection of evolution of monomer conversion versus time (see Figure 1a-d, left) and pseudo-first order kinetics plots (see Figure S1) further implies this is the case. At these feed ratios the \bar{D} was again seen to decrease with increasing $\text{Sc}(\text{OTf})_3$ concentration.

Notably in all the copolymerization examples increasing the concentration of $\text{Sc}(\text{OTf})_3$ affected the relative rate of incorporation of each of the monomer units into the polymer and influenced the overall rate of the reaction; with increased $\text{Sc}(\text{OTf})_3$ concentration an increased incorporation of VAc (presumably due to differences in the interactions between $\text{Sc}(\text{OTf})_3$ with MA or VAc) and a lower overall rate of reaction is observed (see Table S1 and Figure 1b-d and Figure S1b-d).

For comparison the homopolymerization of VAc is well controlled by RAFT agent **8** under the same experimental conditions albeit with low monomer conversion (see Table 1, Entry 13 and Table S1). With $\text{Sc}(\text{OTf})_3$ also present in the reaction mixture the reaction is significantly inhibited/retarded, hence VAc plots are omitted from Figure 1 (see Table 1, Entries 14-15 and Table S1).

From the experiments discussed above it is clear that the inclusion of $\text{Sc}(\text{OTf})_3$ delivers improved control of the RAFT copolymerization of MA and VAc controlled by **8**, particularly with respect to polymer \bar{D} . Additionally the increased rate of chain transfer during copolymerization facilitated by the presence of $\text{Sc}(\text{OTf})_3$ will decrease the level of heterogeneity between the gradient copolymer chains.

Effect of scandium triflate on copolymerization reactivity ratios of methyl acrylate and vinyl acetate

To investigate the effect of $\text{Sc}(\text{OTf})_3$ on the relative reactivity of MA and VAc during their RAFT copolymerization, their reactivity ratios were estimated using non-linear least squares regression fit of copolymerization monomer conversion data.^{4, 6, 35, 45} The evolution of the MA monomer fraction (f_{MA}) with conversion for the three feed ratios in the absence of $\text{Sc}(\text{OTf})_3$ or in the presence of 0.5 and 1 molar equivalents to RAFT agent **8** are shown in Figure 2. The reactivity ratios, r_{MA} and r_{VAc} , obtained from

fitting the integrated copolymer composition equation are shown in Figure 3. The uncertainty in these values is indicated by the joint confidence region contours.

In the absence of $\text{Sc}(\text{OTf})_3$, the reactivity ratios ($r_{\text{MA}} = 4.4$; $r_{\text{VAc}} = 0.038$) indicate a stark preference for MA to homopolymerize and VAc to copolymerize with MA. This is consistent with literature observations.⁴⁶ The result is polymers with very “steep” gradients due to the significant differences in monomer reactivity; in each case without $\text{Sc}(\text{OTf})_3$ the MA reaches full conversion. As the number of molar equivalents of $\text{Sc}(\text{OTf})_3$ to RAFT agent **8** increases to the reactivity ratios are affected, reflecting an increased propensity for MA to copolymerize with VAc and VAc to homopolymerize. In general the “steepness” of the gradient structure within the polymers is decreased and for a given total monomer conversion the extent of incorporation of VAc (F_{VAc}) is increased (see Table 1). This can be appreciated qualitatively by inspection of the differences in the evolution of f_{MA} with total monomer conversion for each $[\text{Sc}(\text{OTf})_3]/[\mathbf{8}]$ ratio (see Figure 2).

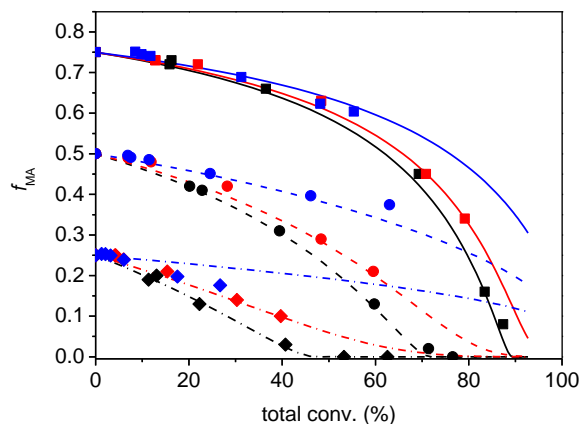


Figure 2: Modelled and measured monomer compositions for $f_{\text{MA,initial}} = 0.75$ (squares, solid lines), 0.5 (circles, dashed lines), and 0.25 (diamonds, dotted lines) with $[\text{Sc}(\text{OTf})_3]:[\mathbf{8}] = 0$ (black lines), $[\text{Sc}(\text{OTf})_3]:[\mathbf{8}] = 0.5$ (red lines) and $[\text{Sc}(\text{OTf})_3]:[\mathbf{8}] = 1.0$ (blue lines). Modelled parameters: $[\text{Sc}(\text{OTf})_3]:[\mathbf{8}] = 0$, $r_{\text{MA}} = 4.4$ and $r_{\text{VAc}} = 0.038$; $[\text{Sc}(\text{OTf})_3]:[\mathbf{8}] = 0.5$, $r_{\text{MA}} = 3.7$ and $r_{\text{VAc}} = 0.21$; $[\text{Sc}(\text{OTf})_3]:[\mathbf{8}] = 1$, $r_{\text{MA}} = 3.3$ and $r_{\text{VAc}} = 0.99$.

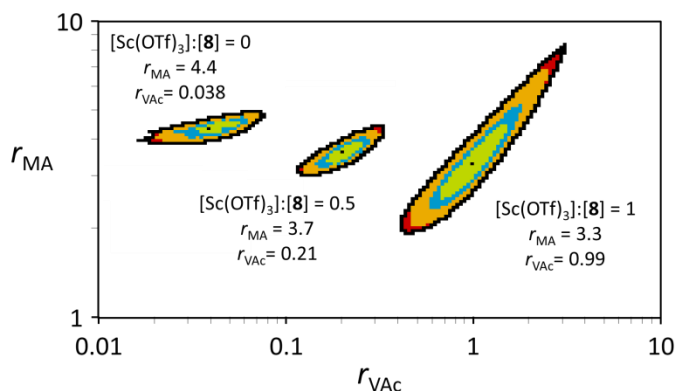
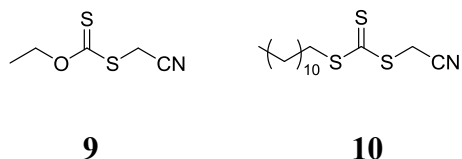


Figure 3: Copolymerization reactivity ratios, r_{MA} and r_{VAc} , and 95% joint confidence regions (JCRs) for RAFT copolymerization of MA and VAc in the presence of **8**, with ratios of $[\text{Sc}(\text{OTf})_3]/[\text{8}]$ of 0, 0.5 and 1. Internal contours represent 50%, 70% and 90% JCRs.

To obtain further insight into the effect of the Lewis acid $\text{Sc}(\text{OTf})_3$ on MA/VAc copolymerization we undertook test experiments under the same reaction conditions with more typical RAFT agents not in possession of a Lewis basic group. These RAFT agents were the cyanomethyl xanthate **9** and the cyanomethyl trithiocarbonate **10** (details of these experiments can be found in the supporting information).



As expected when undertaking the RAFT copolymerization of MA/VAc in the presence of the xanthate **9**, or trithiocarbonate **10** the addition of one molar equivalent of $\text{Sc}(\text{OTf})_3$ to RAFT agent did not affect (reduce) the dispersity to any appreciable extent.‡ An increased rate of incorporation of VAc in relation to MA during earlier stages of polymerization due to interaction of $\text{Sc}(\text{OTf})_3$ with the monomers (in the absence of a Lewis basic group) and slower overall rate of polymerization are observed. The latter may

indicate an overall slower fragmentation of the macroradicals bearing a VAc terminal group and therefore enhanced intermediate radical termination. Indeed the introduction of Sc(OTf)₃ for the RAFT copolymerization of MA/VAc using trithiocarbonate **10** varies from a slow rate of polymerization to significantly retarded by increasing VAc feed (see Table S4 for details); complete inhibition is typically observed when polymerizing VAc in the presence of trithiocarbonates.^{42, 47-48}

Importantly, these experiments also allow the direct comparison between the performance of the switchable RAFT agent **8** (in the presence or absence of Sc(OTf)₃) and more commonly used xanthate and trithiocarbonate RAFT agents (namely **9** and **10** respectively) (see Tables S2 & S4 in the supporting information). In all copolymerization experiments performed in the absence of Sc(OTf)₃ RAFT agent **8** outperformed the xanthate **9**, due to the intrinsic activity of the *N*-aryl-*N*-pyridyl Z group, resulting in polymers of lower *D* (**8**: *D*≈1.3-1.4; **9**: *D*≈1.4-1.7). In the presence of one equivalent of Sc(OTf)₃ to **8** the difference in *D* is even more stark (**8**+Sc(OTf)₃: *D*=1.1-1.3), albeit at high VAc feed retardation of polymerization is evident. In comparison to the trithiocarbonate **10**, RAFT agent **8** in the presence of Sc(OTf)₃ (where [Sc(OTf)₃]/[**8**]=1) gave polymers of lower *D* at similar *M*_n, but at an overall lower rate of conversion.

Copolymer analysis at 50% MA/50% VAc feed ratio

To examine the effect of Sc(OTf)₃ on the polymer microstructure, copolymers were synthesised on preparative scale using a 50% MA/50% VAc feed ratio with 0, 0.5 or 1 molar equivalent of Sc(OTf)₃ to **8** (denoted as **P0**, **P0.5** and **P1** respectively). Reactions were heated at 60°C for 24h to ensure sufficient monomer conversion to facilitate polymer analysis by ¹H NMR (see Figure S4 and S5), ¹³C NMR (Figure 4) and DSC (Figures S3 & S4). Characterisation data is given in Table 2.

Table 2: Characterization data for preparative copolymerization of 50%MA/50%VAc with 8^a

| | [Sc(OTf) ₃] | MA | VAc | Total | F_{MA} | F_{MA} | F_{MA} -centred triads ^{d,e} | | | M_n | M_n | M_n | T_g | |
|---------|-------------------------|-------|-------|-------|----------------------------------|--------------------------|---|------|------|-------------------------------|-----------------------------|--------------------------|-------------|--|
| Polymer | / | conv. | conv. | conv. | F_{MA} (calc.) ^b | (1H NMR) ^c | | | | M_n (calc.) ^f | M_n (GPC) ^g | (1H NMR) ^h | \bar{D}^g | $[T_{g,width}]$ (°C) ^{i,j} |
| | | | | | | | MMM | MMV | VMV | | | | | |
| | | | | | | | [RAFT] | %. | %. | | | | | |
| P0 | 0 | 99 | 38 | 69 | 0.723 | 0.749 | 0.54 | 0.38 | 0.08 | 12200 | 16200 | 13200 | 1.25 | 25.1[10.8] |
| P0.5 | 0.5 | 82 | 21 | 52 | 0.781 | 0.819 | 0.65 | 0.32 | 0.03 | 9360 | 13500 | 12200 | 1.14 | 25.5[11.4] |
| P1 | 1 | 75 | 19 | 47 | 0.798 | 0.842 | 0.63 | 0.30 | 0.07 | 8580 | 11800 | 10500 | 1.15 | 23.3[13.1] |

^a[MA]+[VAc]:[RAFT]:[AIBN] = 200:1.0:0.2, in MeCN, T = 60°C for 24 h, [MA]+[VAc] = 3.33 M; ^bcalculated from monomer conversion data; ^ccalculated from ¹H NMR analysis of purified samples; ^dcalculated from integration of ¹³C NMR resonances of the MA and VAc methine regions^{49¶}; ^d F_{VAc} -centred triads could not be calculated due to insufficient ¹³C NMR sensitivity; ^f M_n (calc.)=([MA]₀ + [VAc]₀)/[RAFT]₀ × ((M_{r,MA} × F_{MA} (calc.)) + (M_{r,VAc} × F_{VAc} (calc.))) × total % conv. + M_{r,RAFT} (where $F_{M(calc)}$ is the calculated mole fraction of monomer in the polymer); ^gGPC DMF eluent, T = 80°C, [LiCl] = 50 mM; ^hcalculated from ¹H NMR analysis; ⁱ T_g peak analysis from first derivative of the DSC heat flow curve; ^jwidth of T_g in parentheses, calculated as per Kim *et al.*⁵

Triad analysis was undertaken by further analysis of the ¹³C NMR spectrum, following the assignments of Brar and Charan,⁵⁰ facilitating investigation of the effect of Sc(OTf)₃ on monomer distributions across the three polymer samples (see Figure 4). Inspection of the VAc methine region of the ¹³C NMR spectra (–CH(V); Figure 4b) indicates a vast predominance of MVM triads indicative of an MA-rich structure for each of the polymer samples. MVV and VVV triads appear to be present albeit in low quantity in **P0** (where MA had reached full conversion), and to a lesser extent in **P0.5** and **P1**. Quantitative analysis of this region could not be conducted because of insufficient spectral sensitivity due to the low mole fraction of VAc in these polymers.

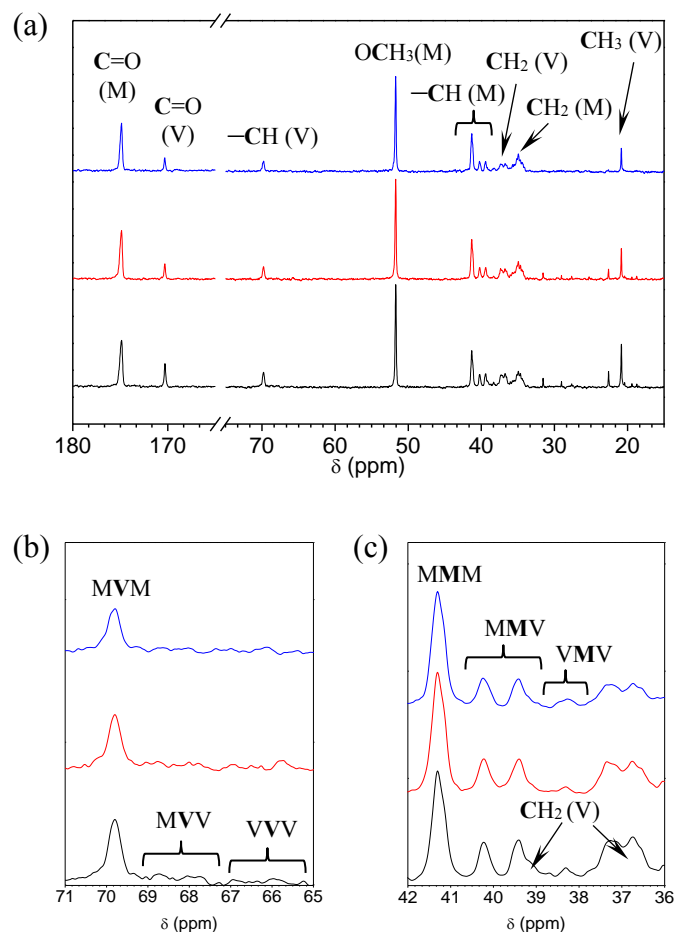


Figure 4: ^{13}C NMR spectra (a) of copolymers **P0** (black), **P0.5** (red) and **P1** (blue) with expansions of the (b) VAc methine ($-\text{CH}$ (V)), and the (c) MA methine ($-\text{CH}$ (M)) regions. (Triad nomenclature: M = MA and V = VAc; bold indicates resonance observed)

Comparison between integrations of the MA methine regions in the ^{13}C NMR spectra of **P1** to **P0.5** (Figure 4c and Table 1) indicates an appreciable increase in the fraction of VMV triads with increased $\text{Sc}(\text{OTf})_3$, indicative of increased incorporation of VAc units into **P1**.[¶] This observation is in agreement with our reactivity ratio observations. **P0** also has more VMV triads than does **P0.5**, likely due to enhanced incorporation of VAc into **P0** at higher total monomer conversion brought about from the increased rate of polymerization in the absence of $\text{Sc}(\text{OTf})_3$.

From DSC analysis of **P0**, **P0.5** and **P1**, each polymer was found to display a single glass transition temperature (T_g) between that of PMA ($\sim 10^\circ\text{C}$)⁴⁶ and PVAc ($\sim 32^\circ\text{C}$)⁴⁶ indicating the absence of microphase separation in bulk phase (see Figures S3 and S4). DSC was unable to provide any demonstrable correlation between the T_g of the copolymers and their composition (see Table 2); the T_g of **P0**, **P0.5** and **P1**, were found to be very similar (see Table 2).

CONCLUSIONS

Herein, we have demonstrated how addition of the Lewis acid $\text{Sc}(\text{OTf})_3$ improves the control over the RAFT copolymerization involving MAMs and LAMs (namely MA and VAc) controlled by an acid/base switchable dithiocarbamate RAFT agent, cyanomethyl (4-fluorophenyl)(pyridin-4-yl)carbamodithioate (**8**), through modulation of its activity.

The introduction of either 0.5 or 1 molar equivalents of $\text{Sc}(\text{OTf})_3$, with respect to RAFT agent **8**, into a RAFT copolymerization of methyl acrylate and vinyl acetate gave substantially improved control resulting in significantly reduced \bar{D} (~ 1.1 - 1.3) when compared to that obtained in its absence (ca. \bar{D} ~ 1.3 - 1.4). Additionally, similar introduction of $\text{Sc}(\text{OTf})_3$ into a homopolymerization of MA mediated by RAFT agent **8** also delivered polymers of low \bar{D} (~ 1.15).

$\text{Sc}(\text{OTf})_3$ was found to reduce the rate of polymerization, and alter the copolymerization reactivity ratios for MA and VAc. Increasing the Lewis acid concentration provided enhanced incorporation of the less active monomer, VAc, into the copolymers (indicated through the change in the reactivity ratios r_{MA} and r_{VAc}). This enhanced VAc incorporation was confirmed by ^{13}C NMR analysis of preparative samples.

High end-group fidelity was observed for all of the RAFT copolymers indicating, importantly, that the inclusion of $\text{Sc}(\text{OTf})_3$ does not deleteriously affect the thiocarbonylthio end-group.

ASSOCIATED CONTENT

Supporting Information. Full experimental conditions and characterization data for kinetic and preparative polymerization reactions, joint confidence internal region plots for reactivity ratio determinations, DSC and ^1H NMR data for polymers **P0**, **P0.5** and **P1**, ^1H NMR spectra of RAFT agents **8**, **9** and **10** with and without $\text{Sc}(\text{OTf})_3$. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

* E-mail: d.keddie@wlv.ac.uk (D.J.K).

NOTES

‡ The ^1H NMR spectrum of RAFT agent **8** in MeCN-d_3 shows a significant shift of the pyridyl resonances in the presence of one molar equivalent of $\text{Sc}(\text{OTf})_3$ from that of **8** alone (see Figure S6). The ^1H NMR spectra of RAFT agents **9** and **10** in MeCN-d_3 show no significant differences whether acquired in the presence or absence of one molar equivalent of $\text{Sc}(\text{OTf})_3$ (see Figures S7 & S8).

¶ Quantitative analysis may be conducted using ^{13}C NMR provided resonances of the same type are compared (in this case methines, CH); see Otte et al.⁴⁹ for further information.

ACKNOWLEDGMENTS

We acknowledge CSIRO Manufacturing and the School of Science and Technology at UNE for funding. D.J.K. also acknowledges the Office of the Chief Executive of CSIRO for an OCE postdoctoral fellowship.

REFERENCES

1. Odian, G., Chain Copolymerization. In *Principles of Polymerization*, John Wiley & Sons, Inc.: 2004; pp 464-543.
2. Matyjaszewski, K.; Ziegler, M. J.; Arehart, S. V.; Greszta, D.; Pakula, T., Gradient copolymers by atom transfer radical copolymerization. *J. Phys. Org. Chem.* **2000**, *13* (12), 775-786.
3. Beginn, U., Gradient copolymers. *Colloid Polym. Sci.* **2008**, *286* (13), 1465-1474.
4. Harriison, S.; Ercole, F.; Muir, B. W., Living spontaneous gradient copolymers of acrylic acid and styrene: one-pot synthesis of pH-responsive amphiphiles. *Polym. Chem.* **2010**, *1* (3), 326-332.
5. Kim, J.; Mok, M. M.; Sandoval, R. W.; Woo, D. J.; Torkelson, J. M., Uniquely Broad Glass Transition Temperatures of Gradient Copolymers Relative to Random and Block Copolymers Containing Repulsive Comonomers. *Macromolecules* **2006**, *39* (18), 6152-6160.
6. Sykes, K. J.; Harriison, S.; Keddie, D. J., Phosphorus-Containing Gradient (Block)Copolymers via RAFT Polymerization and Postpolymerization Modification. *Macromol. Chem. Phys.* **2016**, *217* (20), 2310-2320.
7. Yanez-Macias, R.; Kulai, I.; Ulbrich, J.; Yildirim, T.; Sungur, P.; Hoeppener, S.; Guerrero-Santos, R.; Schubert, U. S.; Destarac, M.; Guerrero-Sanchez, C.; Harriison, S., Thermosensitive spontaneous gradient copolymers with block- and gradient-like features. *Polym. Chem.* **2017**, DOI: 10.1039/C7PY00495H.
8. Keddie, D. J.; Moad, G.; Rizzardo, E.; Thang, S. H., RAFT Agent Design and Synthesis. *Macromolecules* **2012**, *45* (13), 5321-5342.
9. Benaglia, M.; Chiefari, J.; Chong, Y. K.; Moad, G.; Rizzardo, E.; Thang, S. H., Universal (Switchable) RAFT Agents. *J. Am. Chem. Soc.* **2009**, *131* (20), 6914-6915.
10. Keddie, D. J.; Guerrero-Sanchez, C.; Moad, G.; Rizzardo, E.; Thang, S. H., Switchable Reversible Addition-Fragmentation Chain Transfer (RAFT) Polymerization in Aqueous Solution, *N,N*-Dimethylacrylamide. *Macromolecules* **2011**, *44*, 6738-6745.
11. Benaglia, M.; Chen, M.; Chong, Y. K.; Moad, G.; Rizzardo, E.; Thang, S. H., Polystyrene-block-poly(vinyl acetate) through the Use of a Switchable RAFT Agent. *Macromolecules* **2009**, *42* (24), 9384-9386.
12. Stace, S. J.; Moad, G.; Fellows, C. M.; Keddie, D. J., The effect of Z-group modification on the RAFT polymerization of N-vinylpyrrolidone controlled by "switchable" N-pyridyl-functional dithiocarbamates. *Polym. Chem.* **2015**, *6* (40), 7119-7126.
13. Gardiner, J.; Martinez-Botella, I.; Tsanaktsidis, J.; Moad, G., Dithiocarbamate RAFT agents with broad applicability - the 3,5-dimethyl-1H-pyrazole-1-carbodithioates. *Polym. Chem.* **2015**.
14. Gardiner, J.; Martinez-Botella, I.; Kohl, T. M.; Krstina, J.; Moad, G.; Tyrell, J. H.; Coote, M. L.; Tsanaktsidis, J., 4-Halogeno-3,5-dimethyl-1H-pyrazole-1-carbodithioates: versatile reversible addition fragmentation chain transfer agents with broad applicability. *Polym. Int.* **2017**, *66* (11), 1438-1447.
15. Moad, G.; Mayadunne, R. T. A.; Rizzardo, E.; Skidmore, M.; Thang, S., Synthesis of novel architectures by radical polymerization with reversible addition fragmentation chain transfer (RAFT polymerization). *Macromol. Symp.* **2003**, *192*, 1-12.
16. Pound, G.; McKenzie, J. M.; Lange, R. F. M.; Klumperman, B., Polymer-protein conjugates from [small omega]-aldehyde endfunctional poly(N-vinylpyrrolidone) synthesised via xanthate-mediated living radical polymerisation. *Chem. Commun.* **2008**, (27), 3193-3195.
17. Kobayashi, S.; Manabe, K., Development of Novel Lewis Acid Catalysts for Selective Organic Reactions in Aqueous Media. *Acc. Chem. Res.* **2002**, *35* (4), 209-217.

18. Isobe, Y.; Nakano, T.; Okamoto, Y., Stereocontrol during the free-radical polymerization of methacrylates with Lewis acids. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, 39 (9), 1463-1471.
19. Baraki, H.; Habaue, S.; Okamoto, Y., Stereospecific Radical Polymerization of α -(Alkoxymethyl)acrylates Controlled by Lewis Acid Catalysts: Mechanistic Study and Effect of Amino Alcohols as Ligand for Zinc Bromide. *Macromolecules* **2001**, 34 (14), 4724-4729.
20. Suito, Y.; Isobe, Y.; Habaue, S.; Okamoto, Y., Isotactic-specific radical polymerization of methacrylamides in the presence of Lewis acids. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, 40 (14), 2496-2500.
21. Isobe, Y.; Suito, Y.; Habaue, S.; Okamoto, Y., Stereocontrol during the free-radical polymerization of methacrylamides in the presence of Lewis acids. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, 41 (7), 1027-1033.
22. Isobe, Y.; Fujioka, D.; Habaue, S.; Okamoto, Y., Efficient Lewis Acid-Catalyzed Stereocontrolled Radical Polymerization of Acrylamides. *J. Am. Chem. Soc.* **2001**, 123 (29), 7180-7181.
23. Noble, B. B.; Coote, M. L., Chapter Four - Mechanistic Perspectives on Stereocontrol in Lewis Acid-Mediated Radical Polymerization: Lessons from Small-Molecule Synthesis. In *Adv. Phys. Org. Chem.*, Williams, I. H.; Williams, N. H., Eds. Academic Press: 2015; Vol. 49, pp 189-258.
24. Lutz, J.-F.; Jakubowski, W.; Matyjaszewski, K., Controlled/Living Radical Polymerization of Methacrylic Monomers in the Presence of Lewis Acids: Influence on Tacticity. *Macromol. Rapid Commun.* **2004**, 25 (3), 486-492.
25. Ray, B.; Isobe, Y.; Matsumoto, K.; Habaue, S.; Okamoto, Y.; Kamigaito, M.; Sawamoto, M., RAFT Polymerization of N-Isopropylacrylamide in the Absence and Presence of Y(OTf)₃: Simultaneous Control of Molecular Weight and Tacticity. *Macromolecules* **2004**, 37 (5), 1702-1710.
26. Ray, B.; Isobe, Y.; Morioka, K.; Habaue, S.; Okamoto, Y.; Kamigaito, M.; Sawamoto, M., Synthesis of Isotactic Poly(N-isopropylacrylamide) by RAFT Polymerization in the Presence of Lewis Acid. *Macromolecules* **2003**, 36 (3), 543-545.
27. Lutz, J.-F.; Neugebauer, D.; Matyjaszewski, K., Stereoblock Copolymers and Tacticity Control in Controlled/Living Radical Polymerization. *J. Am. Chem. Soc.* **2003**, 125 (23), 6986-6993.
28. Chong, Y. K.; Moad, G.; Rizzardo, E.; Skidmore, M. A.; Thang, S. H., Reversible Addition Fragmentation Chain Transfer Polymerization of Methyl Methacrylate in the Presence of Lewis Acids: An Approach to Stereocontrolled Living Radical Polymerization. *Macromolecules* **2007**, 40 (26), 9262-9271.
29. Rizzardo, E.; Chen, M.; Chong, B.; Moad, G.; Skidmore, M.; Thang, S. H., RAFT Polymerization: Adding to the Picture. *Macromol. Symp.* **2007**, 248 (1), 104-116.
30. Moad, G.; Benaglia, M.; Chen, M.; Chiefari, J.; Chong, Y. K.; Keddie, D. J.; Rizzardo, E.; Thang, S. H., Block Copolymer Synthesis through the Use of Switchable RAFT Agents. In *Non-Conventional Functional Block Copolymers*, Theato, P.; Kilbinger, A. F. M.; Coughlin, E. B., Eds. American Chemical Society: Washington, DC, 2011, ACS Symposium Series; Vol. 1066, pp 81-102.
31. Keddie, D. J.; Guerrero-Sanchez, C.; Moad, G.; Mulder, R. J.; Rizzardo, E.; Thang, S. H., Chain Transfer Kinetics of Acid/Base Switchable N-Aryl-N-Pyridyl Dithiocarbamate RAFT Agents in Methyl Acrylate, N-Vinylcarbazole and Vinyl Acetate Polymerization. *Macromolecules* **2012**, 45 (10), 4205-4215.
32. Liautard, V.; Robert, F. d. r.; Landais, Y., Free-Radical Carboalkynylation and Carboalkenylation of Olefins. *Org. Lett.* **2011**, 13 (10), 2658-2661.
33. Gupta, J.; Keddie, D. J.; Wan, C.; Haddleton, D. M.; McNally, T., Functionalisation of MWCNTs with poly(lauryl acrylate) polymerised by Cu(0)-mediated and RAFT methods. *Polym. Chem.* **2016**.

34. Gottlieb, H. E.; Kotlyar, V.; Nudelman, A., NMR chemical shifts of common laboratory solvents as trace impurities. *J. Org. Chem.* **1997**, *62* (21), 7512-7515.
35. Guerrero-Sanchez, C.; Harrisson, S.; Keddie, D. J., High-Throughput Method for RAFT Kinetic Investigations and Estimation of Reactivity Ratios in Copolymerization Systems. *Macromol. Symp.* **2013**, *325-326* (1), 38-46.
36. Guerrero-Sanchez, C.; O'Brien, L.; Brackley, C.; Keddie, D. J.; Saubern, S.; Chiefari, J., Quasi-block copolymer libraries on demand via sequential RAFT polymerization in an automated parallel synthesizer. *Polym. Chem.* **2013**, *4* (6), 1857-1862.
37. Haven, J. J.; Guerrero-Sanchez, C.; Keddie, D. J.; Moad, G., Rapid and Systematic Access to Quasi-Diblock Copolymer Libraries Covering a Comprehensive Composition Range by Sequential RAFT Polymerization in an Automated Synthesizer. *Macromol. Rapid Commun.* **2014**, *35* (4), 492-497.
38. Haven, J. J.; Guerrero-Sanchez, C.; Keddie, D. J.; Moad, G.; Thang, S. H.; Schubert, U. S., One pot synthesis of higher order quasi-block copolymer libraries via sequential RAFT polymerization in an automated synthesizer. *Polym. Chem.* **2014**, *5* (18), 5236-5246.
39. Hinton, T. M.; Guerrero-Sanchez, C.; Graham, J. E.; Le, T.; Muir, B. W.; Shi, S.; Tizard, M. L. V.; Gunatillake, P. A.; McLean, K. M.; Thang, S. H., The effect of RAFT-derived cationic block copolymer structure on gene silencing efficiency. *Biomaterials* **2012**, *33* (30), 7631-7642.
40. Guerrero-Sanchez, C.; Keddie, D. J.; Saubern, S.; Chiefari, J., Automated Parallel Freeze–Evacuate–Thaw Degassing Method for Oxygen-Sensitive Reactions: RAFT Polymerization. *ACS. Comb. Sci.* **2012**, *14* (7), 389-394.
41. Destarac, M.; Charmot, D.; Franck, X.; Zard, S. Z., Dithiocarbamates as universal reversible addition-fragmentation chain transfer agents. *Macromol. Rapid Commun.* **2000**, *21*, 1035-1039.
42. Harrisson, S.; Liu, X.; Ollagnier, J.-N.; Coutelier, O.; Marty, J.-D.; Destarac, M., RAFT polymerization of vinyl esters: Synthesis and applications. *Polymers* **2014**, *6* (5), 1437-1488.
43. Malepu, V.; Petruczuk, C. D.; Tran, T.; Zhang, T.; Thopasridharan, M.; Shipp, D. A., RAFT Polymerization of Vinyl Acetate, Styrene and Acrylates Using *N,N*-Dithiocarbamates. In *Controlled/Living Radical Polymerization: Progress in RAFT, DT, NMP & OMRP*, Matyjaszewski, K., Ed. American Chemical Society: 2009; Vol. 1024, pp 37-47.
44. Dayter, L. A.; Murphy, K. A.; Shipp, D. A., RAFT Polymerization of Monomers with Highly Disparate Reactivities: Use of a Single RAFT Agent and the Synthesis of Poly(styrene-block-vinyl acetate). *Aust. J. Chem.* **2013**, *66* (12), 1564-1569.
45. Van Den Brink, M.; Van Herk, A. M.; German, A. L., Nonlinear regression by visualization of the sum of residual space applied to the integrated copolymerization equation with errors in all variables. I. Introduction of the model, simulations and design of experiments. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37* (20), 3793-3803.
46. Brandrup, J.; Immergut, E. H.; Grulke, E. A., *Polymer Handbook*. Fourth ed.; Wiley: New York, 1999.
47. Moad, G.; Rizzardo, E.; Thang, S. H., Living Radical Polymerization by the RAFT Process. *Aust. J. Chem.* **2005**, *58* (6), 379-410.
48. Postma, A.; Davis, T. P.; Li, G.; Moad, G.; O'Shea, M., RAFT Polymerization with Phthalimidomethyl Trithiocarbonates or Xanthates. On the Origin of Bimodal Molecular Weight Distributions in Living Radical Polymerization. *Macromolecules* **2006**, *39*, 5307-5318.
49. Otte, D. A. L.; Borchmann, D. E.; Lin, C.; Weck, M.; Woerpel, K. A., ¹³C NMR Spectroscopy for the Quantitative Determination of Compound Ratios and Polymer End Groups. *Org. Lett.* **2014**, *16* (6), 1566-1569.
50. Brar, A. S.; Charan, S., Sequence determination of vinyl acetate-methyl acrylate copolymers by NMR spectroscopy. *J. Appl. Polym. Sci.* **1994**, *53*, 1813-22.

